Neuroimaging measure as an endophenotype for genetic effects on electrical stimulation in Brown Norway and Dahl salt-sensitive rat strains

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Introduction: The association of a specific behavioral outcome with a specific gene variant has been weak and controversial. However, the penetrance of gene effects at the level of brain biology is more obvious and consistent than that at the level of behavioral phenotypes. Neuroimaging genetics techniques have provided a unique tool to explore and evaluate the phenotypic impact of brain-relevant genetic polymorphisms longitudinally and noninvasively. The goal of this study was to reveal the region-specific effects of genetic differences between two inbred rat strains, Brown Norway (BN) and Dahl salt-sensitive (SS/Mcwii), on a biologic measure in brain using BOLD-fMRI under a well-established task paradigm.

Materials and Methods: Animal Strain: Thirteen male BN, ten male SS and nine male SS-13th/Mcwii consomic rats were used for this study. All rats were maintained on regular dietary before BOLD-fMRI experiments. When formulated at 2 mA D/C, mechanical ventilation was used for anesthesia under different sensitivity to stimulations, but also for the altered somatosensory neuropathway. These results suggest a new approach to the comprehensive assessment of task-relevant BOLD-fMRI activation, we believe that there are likely to be genetic components responsible not only for the different sensitivity to stimulations, but also for the altered somatosensory neuropathway. These results suggest a new approach to visualize the genetic effects on the brain using neuroimaging measures.

Results: While left forepaw stimuli with different frequencies induced robust positive activations in contralateral primary somatosensory cortex (S1FL) in both SS (Figure a) and BN(Figure b) groups, BN rats showed a significant increased activate volume(voxel numbers) in S1FL regions under different frequencies. The activation foci showed an increased spatial distribution within S1FL with the increased stimulus frequencies in each group (P<0.005 with correction). Two-sample t-test was used to determine the group-level difference patterns between groups (P<0.05 with correction). The numbers of activated voxels that survived the threshold and their BOLD percentage changes were further analyzed with rat body weight and age as covariates(1)

Discussion and Conclusion: Inbred rat strains have been widely used in the development of physiological and pathophysiological models to study human disease because of the less interanimal variation. Striking differences among rat strains have been found in resistance to myocardial injury, sensitivity to painful stimuli, and neuroprotectivity to cerebral ischemia as well as other neurological disorders(2). In the current study, we demonstrated robust differences in response to a well-established electrical stimulus paradigm in two inbred rat strains by BOLD-fMRI. By minimizing the confounding environmental influences and controlling the effects of rat age and body weight, SS rats exhibited less activation volumes in somatosensory cortex at different frequencies compared to BN rats, although the BOLD percent changes were not significantly different between two groups. Based on the comprehensive assessment of task-relevant BOLD-fMRI activation, we believe that there are likely to be genetic components responsible not only for the different sensitivity to stimulations, but also for the altered somatosensory neuropathway. These results suggest a new approach to visualize the genetic effects on the brain using neuroimaging measures.

Figure. Left forepaw stimulation-induced BOLD activations at different frequencies. Activation maps are overlaid on ideal anatomical images. Positive BOLD responses are in warm color, and negative BOLD responses are in cold color. (a) Activation maps of SS group. (b) Activation maps of BN group. (c) Group-level differential activation maps between SS and BN groups. (d) Numerical presentation of activated volume (left) and percent changes of BOLD signals. (*p < 0.05). Primary somatosensory cortex (1), Secondary somatosensory cortex(2), Caudate Putamen(3), Primary somatosensory cortex- Barrel field(4), Thalamus(5).


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